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**TRANSMITTAL LETTER TO THE UNITED STATES
DESIGNATED/ELECTED OFFICE (DO/EO/US)
CONCERNING A FILING UNDER 35 U.S.C. 371**

ATTORNEY'S DOCKET NUMBER

06082.0026

U.S. APPLICATION NO
(If known, see 37 CFR 1.5)**09/936166**

INTERNATIONAL APPLICATION NO.

PCT/JP00/01443

INTERNATIONAL FILING DATE

March 9, 2000

PRIORITY DATE CLAIMED

March 11, 1999


TITLE OF INVENTION**RADIOACTIVE MICROSPHERES EXCELLENT IN CHEMICAL DURABILITY AND METHOD FOR
MANUFACTURING THE SAME****APPLICANT(S) FOR DO/EO/US**Tadashi KOKUBO, Masakazu KAWASHITA, Masahiro HIRAOKA, Yasushi NAGATA, Yoshiaki INOUE, Takao
YAMAZAKI, Yasuhiro SHIMIZU, and Yoshiki SAWADA

Applicant(s) herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☒ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371 (c)(2)).
 - a. ☐ is attached hereto (required only if not communicated by the International Bureau).
 - b. ☒ has been communicated by the International Bureau.
 - c. ☐ is not required, as the application was filed with the United States Receiving Office (RO/US).
6. ☒ An English language translation of the International Application as filed (35 U.S.C. 371 (c)(2)).
 - a. ☒ is attached hereto.
 - b. ☐ has been previously submitted under 35 U.S.C. 154 (d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371 (c)(3)).
 - a. ☐ are attached hereto (required only if not communicated by the International Bureau).
 - b. ☐ have been communicated by the International Bureau.
 - c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
 - d. ☒ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371 (c)(4)).
10. ☐ An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371 (c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. ☒ Information Disclosure Statement under 37 CFR 1.97 and 1.98
12. ☒ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ A **FIRST** preliminary amendment.
14. ☐ A **SECOND** or **SUBSEQUENT** preliminary amendment.
15. ☐ A Substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821-1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154 (d)(4).
19. ☐ A second copy of the English language translation of the international application 35 U.S.C. 154 (d)(4).
20. ☒ Other items or information:
 - a. ☒ Copy of cover page of International Publication No. WO00/54284
 - b. ☐ Copy of Notification of Missing Requirements.
 - c. ☐

U.S. APPLICATION NO. (If known, see 37 CFR 1.5) 09/936166		INTERNATIONAL APPLICATION NO. PCT/JP00/01443		ATTORNEY'S DOCKET NUMBER 06082.0026	
21. <input checked="" type="checkbox"/> The following fees are submitted:				CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):					
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO				\$1000.00	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO				\$860.00	
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search fee (37 CFR 1.445(a)(2)) paid to USPTO				\$710.00	
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4)				\$690.00	
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33 (1)-(4)				\$100.00	
ENTER APPROPRIATE BASIC FEE AMOUNT =				\$860.00	
Surcharge of \$130.00 for furnishing the oath or declaration later than months from the earliest claimed priority date (37 CFR 1.492 (e)). <input type="checkbox"/> 20 <input type="checkbox"/> 30				\$	
CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total Claims	19	- 20 =	x \$18.00	\$	
Independent Claims	3	-3 =	x \$80.00	\$	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+\$270.00	\$270.00	
TOTAL OF THE ABOVE CALCULATIONS =				\$1130.00	
<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2.				\$	
SUBTOTAL =				\$1130.00	
Processing fee of \$130.00 for furnishing the English translation later than months from the earliest priority date (37 CFR 1.492(f)). <input type="checkbox"/> 20 <input type="checkbox"/> 30				\$	
TOTAL NATIONAL FEE =				\$1130.00	
Fee for recording the enclosed assignment (37 CFR 1.21 (h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property.				+\$40.00	
TOTAL FEES ENCLOSED =				\$1170.00	
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a. <input checked="" type="checkbox"/> A check in the amount of \$ <u>1170.00</u> to cover the above fees is enclosed.					
b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.					
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DATED: September 10, 2001				 SIGNATURE Ernest F. Chapman Reg. No. 25,961 NAME/REGISTRATION NO.	

2/PATS₁

533 Rec'd PCT/PTO 10 SEP 2001
09/936166

SPECIFICATION

RADIOACTIVE MICROSPHERES EXCELLENT IN CHEMICAL DURABILITY AND METHOD FOR MANUFACTURING THE SAME

5

Technical Field

The present invention relates to radioactive microspheres excellent in chemical durability, in particular microspheres favorably applicable for treating affected regions of a cancer patient by directly irradiating the regions with a radiation after injecting the radioactive microspheres into the patient's body.

Background Art

The therapeutic methods for irradiating affected regions with a radiation for treating a cancer have an advantage that functional recoveries of organs can be expected over surgical methods by which the organs are excised. Among the methods described above, use of a therapeutic method for directly irradiating tumors with a radiation by injecting radioactive microspheres into the affected region through the blood vessel by means of a catheter is thought to be promising, since a sufficient dosage of radiation can be irradiated to the affected region without damaging normal tissues just under the surface of the body, as compared with a therapeutic method by which

the radiation is irradiated from the outside of the body.

However, the radioactive microspheres with a too large particle size may be detained before they arrive at the affected region, while those with a too small particle size will penetrate through capillary blood vessels to fail in retaining them at the affected region. When the microspheres are readily dissolved in the body, on the other hand, radioactive elements are transferred to other portions in the body and normal cells are also damaged. A too long half-life also damages the normal tissues by emitting radioactive rays after the therapy, and a too short half-life causes a rapid decay of radioactivity to make the therapy unavailable. From these situations, the microspheres are required to have a diameter of 1 to 100 μm , preferably 20 to 30 μm , to be excellent in chemical durability, and to have a proper half-life.

Materials to be used for the conventional microspheres include an yttria-alumina-silica glass or a glass containing a small amount of phosphorous, wherein the non-radioactive element yttrium or phosphorous in the glass is converted into a β -emitter yttrium or phosphorous by irradiating slow neutrons (Japanese Patent Application Publication No. 6-62439). The glass named as YAS-4 in the patent publication and having a composition ratio of Y_2O_3 : Al_2O_3 : SiO_2 = 40 : 20 : 20 in % by weight (Y_2O_3 : Al_2O_3 : SiO_2 = 19 : 17 : 64 in mol%) has a most excellent chemical

durability among the substances disclosed in the patent, and the microspheres having a proper particle size can be manufactured by a usual melting method.

Since β -emitter yttrium has a half-life as short as
5 64.1 hours, its radioactivity is remarkably decayed during transportation to a hospital after irradiating neutrons in a nuclear reactor. Accordingly, it is required for using the glass microspheres described in Japanese Patent Application Publication No. 6-62439 that the glass spheres
10 contain as much yttria as possible.

However, the content of yttria is naturally restricted within a range capable of forming a glass, since the microspheres described in the patent publication is formed after manufacturing the glass. Since a large
15 quantity of lactic acid is secreted at the tumors, pH in the vicinity of the microspheres is conjectured to be substantially low. The glass described in the patent publication above has a tendency that its chemical durability decreases as the content of yttria turns out to
20 be high.

Phosphorous is also converted from a non-radioactive element to a β -emitter as in the case of yttrium by irradiating with slow neutrons. The β -emitter phosphorous has a considerably longer half-life of 14.3 days.

25 However, a glass containing a large quantity of phosphorous while being excellent in chemical durability

has not been developed yet. Phosphorous in the currently available glass containing a large quantity of phosphorous is rapidly dissolved out of the glass in the body.

Accordingly, the object of the present invention is
5 to provide microspheres being excellent in chemical durability, emitting a radiation for a long period of time in the body, and having a diameter of 1 to 100 μm .

Disclosure of Invention

10 Radioactive microspheres for attaining the object of the present invention comprise not less than 99% by weight of an oxide crystal containing 47% by weight or more of radioactive yttrium, and the balance of inevitable impurities.

15 The conventional yttria-alumina-silica glass (with a composition ratio of $\text{Y}_2\text{O}_3 : \text{Al}_2\text{O}_3 : \text{SiO}_2 = 40 : 20 : 40$ in % by weight) contains yttrium in a proportion of 31.5 % by weight ($40 \times 88.91 \times 2/225.82$). On the contrary, the radioactive microspheres according to the present invention
20 having the composition as described above contain yttrium in a proportion of $47\% \times 0.99 = 46.5\%$ by weight or more, which is by 1.47 times as much as the yttrium content in the conventional glass. Accordingly, the remaining content of radioactive yttrium amounts 1.47 times as high
25 as the radioactive yttrium in the conventional glass even after the half-life.

Since the weight fraction of yttrium in yttria is $88.91 \times 2/225.82$ when the oxide crystal is represented by Y_2O_3 , the yttrium content is 78 % by weight or more, which is 2.47 times as high as the yttrium content in the conventional glass. Accordingly, a radiation with a dosage by 2.47 times as large as that of the conventional glass can be irradiated on the affected region.

The oxide crystal may be YPO_4 , or a mixture of Y_2O_3 and YPO_4 . While the lower limit of the yttrium content in the entire microspheres decreases to 48 % by weight when the oxide crystal is represented by YPO_4 , the Y content remains to be higher than the conventional glass. Furthermore, since phosphorous having a substantially longer half-life is involved in place, radioactivity is additionally increases.

The radioactive microspheres according to the present invention may be coated with a film comprising at least one of the compounds selected from silica (SiO_2), titania (TiO_2), alumina (Al_2O_3), iron (III) oxide (Fe_2O_3), silicon nitride (Si_2N_3 , SiN , Si_3N_4), aluminum nitride (AlN), titanium nitride (TiN), iron nitride (Fe_2N , Fe_4N), silicon carbide (SiC) and titanium carbide (TiC). Since these coating films do not emit harmful α - or γ -ray after irradiating with neutrons while having an acid resistant property, the radioactive elements are not dissolved in the strongly acidic body fluid at the tumors to enable a long

irradiation of the tumor with the radiation. The preferable thickness of the coating film is 0.01 to 5 μm . When the thickness is less than 0.01 μm , erosion of acids is not effectively prevented while, when the thickness exceeds 5 μm , the proportion of yttrium in the entire microspheres becomes too small. Silica is the most preferable material for forming the coating film.

An appropriate method for manufacturing the microspheres according to the present invention is as follows.

At first, an oxide powder as a starting material containing yttrium, or yttrium and phosphorous, is melted by allowing the powder to pass through a thermal-plasma to obtain microspheres containing non-radioactive yttrium (or yttrium and phosphorous). The powder material can be melted, for example, by allowing it to pass through a thermal-plasma or laser beam. Yttria may be efficiently formed into spheres by the high temperature of the thermal-plasma, and phosphorous components in yttrium phosphate is not decomposed since the thermal-plasma is a heat source that does not use reactive gases such as oxygen and steam. However, the heating means are not restricted to the thermal-plasma and laser beam. Then, yttrium (or yttrium and phosphorous) is (are) turned into a radioactive element (elements) by irradiating with an effective dosage of neutrons. In order to enhance chemical durability, it

is recommended to heat the microspheres in an oxidizing atmosphere before irradiating with the neutrons.

For forming the oxide coating film on the surface, the microspheres and a starting material of the coating film are placed in a plasma polymerization apparatus to form the coating film on the surface of the microspheres by plasma polymerization, followed by irradiating an effective dosage of neutrons to yttrium (or yttrium and phosphorous). Si, Ti, Al, Fe, O, N and C constituting the coating film are preferable as the coating film materials since they do not emit harmful radiation (α -ray and γ -ray) by being irradiated with neutrons. While plasma polymerization is one example of the methods for forming the coating film, other methods such as a sputtering method, a vacuum deposition method, a deposition method from solution, a chemical vapor deposition method, a molecular beam epitaxy method, ion-beam vapor deposition method and a sol-gel method may be used.

Brief Description of the Drawings

Fig. 1 describes a condition for forming the coating film on the substrate by plasma polymerization.

Fig. 2 shows a SEM photograph for observing the spherical shapes of the microspheres before and after forming the coating film.

Best Mode for Carrying Out the Invention

EXAMPLE 1

A fine powder containing 99.9 % by weight of yttria was melted with a high frequency induction thermal-plasma under the following condition to form into spheres.

Powder feed carrier gas: Ar 5L/min

Plasma gas composition: Ar 90 L/min + O₂ 5L/min

High frequency generator: anode input 40 kW,

output frequency 4 MHz

A group of the microspheres were dispersed in ultra pure water with a specific conductance of 18 MΩ·cm, and classified with a nylon sieve to obtain microspheres containing not less than 99 % by weight of Y₂O₃ and having a diameter of 20 to 30 μm. The microspheres obtained were subjected to the following chemical durability test.

The microspheres (0.2g) were placed in a polypropylene bottle together with 20 ml of distilled water and, while maintaining the water temperature at 95°C in an oil bath, the bottle was shaken for 7 days with a stroke length of 3 cm at a speed of 120 strokes/min. After filtering the solution, the yttrium content in the filtrate was assayed by a high frequency inductively coupled plasma atomic emission spectrometry (ICP). The result showed that the proportion of dissolved yttrium is 1 ppm or less.

COMPARATIVE EXAMPLE 1

The chemical durability test was carried out under

the same condition as in Example 1, except that a glass with a composition ratio of $Y_2O_3 : Al_2O_3 : SiO_2 = 40 : 20 : 20$ was used for the radioactive microspheres, in place of the microspheres in Example 1. The result showed that the proportion of dissolved yttrium is 6 ppm.

A comparison of the result in Example 1 with the result in Comparative Example 1 shows that the microspheres comprising yttria according to the present invention are superior to the glass microspheres in chemical durability.

10 EXAMPLE 2

Microspheres containing 99 % by weight or more of YPO_4 and having a diameter of 20 to 30 μm were manufactured by the same method as in Example 1 for manufacturing the yttria microspheres. These microspheres were heated at 900°C in the atmosphere for four hours.

The microspheres after heating were subjected to the same chemical durability test as in Example 1. The result showed that the proportion of dissolved yttrium and dissolved phosphorous were 1.2 ppm and 1.7 ppm, respectively. When the same chemical durability test was applied to the microspheres before heating in the atmosphere, the proportion of dissolved yttrium and dissolved phosphorous were 0.73 ppm and 85 ppm, respectively.

Accordingly, it was made clear that chemical durability is remarkably improved by heat treating the microspheres comprising the oxide crystal according to the

present invention, even when the microspheres contain phosphorous that is liable to be readily dissolved out.

EXAMPLE 3

Microspheres (0.6g) obtained by the same
5 manufacturing method as in Example 1 and containing 99 %
by weight or more of Y_2O_3 , with a diameter of 20 to 30 μm were
placed in a polystyrene container with a size of 20 \times 20
 \times 5 mm³. The container was placed in a plasma polymerization
apparatus (Model BP-2, made by Samco International
10 Research Laboratories, Co.) as shown in Fig. 1 to coat the
surface of the microspheres with a SiO_2 film. Tetraethoxy
silane (made by Shinetsu Chemical Industry Co.) was used
as the starting material of SiO_2 , oxygen was used as the
reactive gas, and argon was used as a carrier gas. The
15 conditions in this example were: inner pressure of the
reaction chamber - 0.6 Torr; output - 1.0 w/cm^2 ; oxygen gas
flow rate - 200 ml/min⁻¹, argon gas flow rate - 20 ml/min⁻¹;
and electrode temperature - 20°C. For uniformly coating
the entire surface of the microspheres, the film deposition
20 time was adjusted to 15 minutes per one film deposition run,
the polystyrene container was shaken after the first film
deposition run, and the film deposition process was repeated
again. The film deposition was repeated 4 times in total.

The microspheres coated with the SiO_2 film were
25 observed under a scanning electron microscope (SEM, Model
S-2500CX, made by Hitachi, Ltd.) to compare the coated

microspheres with those before coating. The result in Fig. 2 showed that the shape was not changed even after coating, indicating that the coating film can be formed on the surface without changing the shape of the microspheres.

5 The microspheres with the coating film was subjected to the chemical durability test under the same condition as in Example 1, showing that the proportion of dissolved yttrium was 1 ppm or less.

EXAMPLE 4

10 The chemical durability test was applied to the microspheres with the coating film in Example 3 by the same condition as in Example 3, except that a buffer solution with pH 4 (0.05 M potassium hydrogen phthalate ($C_6H_4(COOK)(COOH)$) was used in place of distilled water.

15 The assay result showed that the proportion of dissolved yttrium was 3 ppm.

REFERENCE EXAMPLE

20 The chemical durability test was applied to the microspheres used in Example 1 under the same condition as in Example 4 without forming the coating film. The result showed that the proportion of dissolved yttrium reaches 120 ppm.

COMPARATIVE EXAMPLE 2

25 The chemical durability test was applied to the glass microspheres used in Comparative Example 1 under the same condition as used in Example 4. The assay result showed

that the proportion of dissolved yttrium was 1.59×10^3 ppm.

Comparisons of the results in Examples 3 and 4 with the results in Reference Example and Comparative Example 2 showed that acid resistance remarkably increases by forming the coating film on the surface of the microspheres.

Industrial Applicability

The radioactive microspheres of the present invention as hitherto described contains a high concentration of radioactive elements that are hardly dissolved. Accordingly, the microspheres are useful as a medical material for treating tumors by direct irradiation of radiation by embedding the microspheres in the vicinity of the tumors.

CLAIMS

1. A radioactive microsphere comprising not less than 99% by weight of an oxide crystal containing 47% by weight or
5 more of radioactive yttrium, and the balance of inevitable impurities.

2. The radioactive microsphere according to claim 1, wherein the oxide crystal consists essentially of Y_2O_3 .

10

3. The radioactive microsphere according to claim 1, wherein the oxide crystal consists essentially of YPO_4 , or a mixture of Y_2O_3 and YPO_4 .

15

4. The radioactive microsphere according to claim 1, wherein the microsphere has a diameter of 1 to 100 μm .

5. The radioactive microsphere according to claim 1, wherein the microsphere has a diameter of 20 to 30 μm .

20

6. The radioactive microsphere according to any one of claims 1 to 5, wherein the microsphere is coated with a film comprising at least one of the compounds selected from silica (SiO_2), titania (TiO_2), alumina (Al_2O_3), iron (III) oxide (Fe_2O_3), silicon nitride (Si_2N_3 , SiN , Si_3N_4), aluminum
25 nitride (AlN), titanium nitride (TiN), iron nitride (Fe_2N ,

Fe₄N), silicon carbide (SiC) and titanium carbide (TiC).

7. The radioactive microsphere according to claim 6, wherein the film has a thickness of 0.01 to 5 μ m.

5

8. A method of producing a radioactive microsphere, the method comprising preparing a microsphere comprising not less than 99% by weight of an oxide crystal containing 47% by weight or more of non-radioactive yttrium, and the
10 balance of inevitable impurities through melting of a starting material, followed by irradiating with an effective dosage of slow neutrons to turn non-radioactive yttrium into a radioactive element.

15 9. A method of producing a radioactive microsphere, the method comprising preparing a microsphere comprising not less than 99% by weight of an oxide crystal containing 47% by weight or more of non-radioactive yttrium and an amount of phosphorous, and the balance of inevitable impurities
20 through melting of a starting material, followed by heating the microsphere in an oxidizing atmosphere and then irradiating with an effective dosage of slow neutrons to turn non-radioactive yttrium into a radioactive element.

25 10. The method according to claim 8 or 9, further comprising coating the microsphere with a film after preparing the

microsphere or heating in the oxidizing atmosphere and before irradiating with an effective dosage of slow neutrons, the film comprising at least one of the compounds selected from silica (SiO_2), titania (TiO_2), alumina (Al_2O_3), iron
5 (III) oxide (Fe_2O_3), silicon nitride (Si_2N_3 , SiN , Si_3N_4), aluminum nitride (AlN), titanium nitride (TiN), iron nitride (Fe_2N , Fe_4N), silicon carbide (SiC) and titanium carbide (TiC).

ABSTRACT

A microsphere which is excellent in chemical durability and capable of emitting a radiation for a long period of time in the body, and has a diameter of 1 to 100 μm , characterized in that it comprises not less than 99% by weight of an oxide crystal containing 47% by weight or more of radioactive yttrium, such as Y_2O_3 and YPO_4 and the balance of inevitable impurities.

FIG. 1

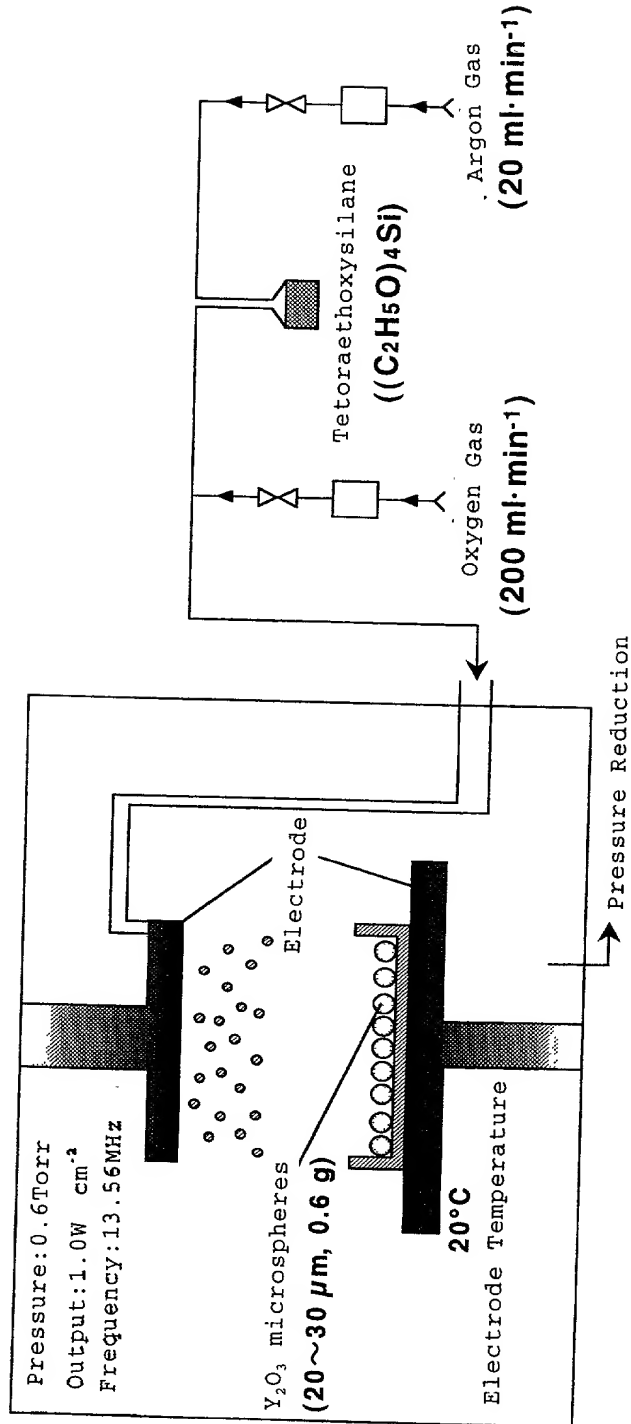
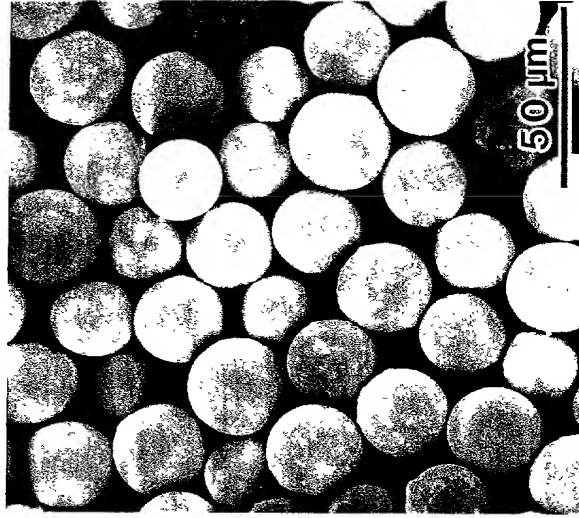
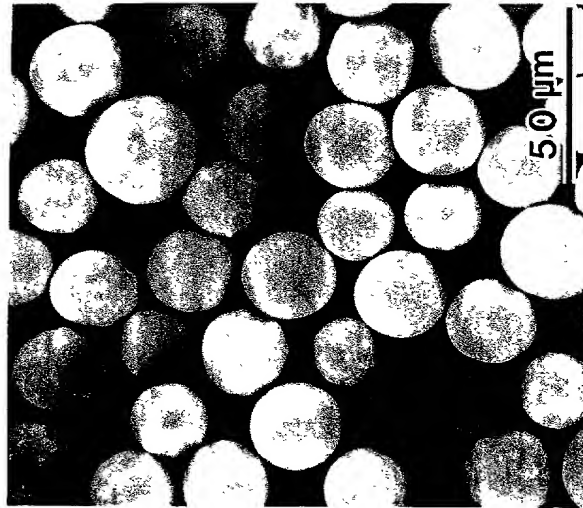


FIG. 2

AFTER FORMING THE COATING FILM



BEFORE FORMING THE COATING FILM



DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that: My residence, post office address and citizenship are as stated below next to my name; I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**RADIOACTIVE MICROSPHERES EXCELLENT IN CHEMICAL DURABILITY
AND METHOD FOR MANUFACTURING THE SAME**

the specification of which:

is attached hereto; or

was filed as United States Application Serial No. _____

on _____ and was amended

on _____ (if applicable); or

was filed as PCT International Application Number PCT/JP00/01443

on _____ and was amended

on _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56.

I hereby claim foreign priority benefits under 35 U.S.C. § 119(a)-(d) or § 365(b) of any foreign application(s) for patent or inventor's certificate or § 365(a) of any PCT international application(s), designating at least one country other than the United States, listed below and have also identified below any foreign application(s) for patent or inventor's certificate, or any PCT international application(s) having a filing date before that of the application(s) of which priority is claimed:

Country	Application Number	Date of Filing	Priority Claimed Under 35 U.S.C. 119
Japan	H11/64758	March 11, 1999	X YES <input type="checkbox"/> NO
			X YES <input type="checkbox"/> NO
			X YES <input type="checkbox"/> NO
			X YES <input type="checkbox"/> NO
			X YES <input type="checkbox"/> NO
			X YES <input type="checkbox"/> NO
			YES <input type="checkbox"/> NO

I hereby claim the benefit under 35 U.S.C. § 119(e) of any United States provisional application(s) listed below:

Application Number	Date of Filing

I hereby claim the benefit under 35 U.S.C. § 120 of any United States application(s) or § 365(c) of any PCT international application(s) designating the United States, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT international application(s) in the manner provided by the first paragraph of 35 U.S.C. § 112, I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR § 1.56 which became available between the filing date of the prior application(s) and the national or PCT international filing date of this application:

Application Number	Date of Filing	Status (Patented, Pending, Abandoned)

I hereby appoint the following attorney and/or agent(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith. **FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P., Reg. No. 22,540**, Douglas B. Henderson, Reg. No. 20,291; Ford F. Farabow, Jr., Reg. No. 20,630; Arthur S. Garrett, Reg. No. 20,338; Donald R. Dunner, Reg. No. 19,073; Brian G. Brunsvold, Reg. No. 22,593; Tipton D. Jennings IV, Reg. No. 20,645; Jerry D. Voight, Reg. No. 23,020; Laurence R. Hefter, Reg. No. 20,827; Kenneth E. Payne, Reg. No. 23,098; Herbert H. Mintz, Reg. No. 26,691; C. Larry O'Rourke, Reg. No. 26,014; Albert J. Santorelli, Reg. No. 22,610; Michael C. Elmer, Reg. No. 25,857; Richard H. Smith, Reg. No. 20,609; Stephen L. Peterson, Reg. No. 26,325; John M. Romary, Reg. No. 26,331; Bruce C. Zotter, Reg. No. 27,680; Dennis P. O'Reilly, Reg. No. 27,932; Allen M. Sokal, Reg. No. 26,695; Robert D. Bajefsky, Reg. No. 25,387; Richard L. Stroup, Reg. No. 28,478; David W. Hill, Reg. No. 28,220; Thomas L. Irving, Reg. No. 28,619; Charles E. Lipsey, Reg. No. 28,165; Thomas W. Winland, Reg. No. 27,605; Basil J. Lewis, Reg. No. 28,818; Martin I. Fuchs, Reg. No. 28,508; E. Robert Yoches, Reg. No. 30,120; Barry W. Graham, Reg. No. 29,924; Susan Haberman Griffen, Reg. No. 30,907; Richard B. Racine, Reg. No. 30,415; Thomas H. Jenkins, Reg. No. 30,857; Robert E. Converse, Jr., Reg. No. 27,432; Clair X. Mullen, Jr., Reg. No. 20,348; Christopher P. Foley, Reg. No. 31,354; John C. Paul, Reg. No. 30,413; David M. Kelly, Reg. No. 30,953; Kenneth J. Meyers, Reg. No. 25,146; Carol P. Einaudi, Reg. No. 32,220; Walter Y. Boyd, Jr., Reg. No. 31,738; Steven M. Anzalone, Reg. No. 32,095; Jean B. Fordis, Reg. No. 32,984; Barbara C. McCurdy, Reg. No. 32,120; James K. Hammond, Reg. No. 31,964; Richard V. Burgujian, Reg. No. 31,744; J. Michael Jakes, Reg. No. 32,824; Dirk D. Thomas, Reg. No. 32,600; Thomas W. Banks, Reg. No. 32,719; Christopher P. Isaac, Reg. No. 32,616; Bryan C. Diner, Reg. No. 32,409; M. Paul Barker, Reg. No. 32,013; Andrew Chanho Sonu, Reg. No. 33,457; David S. Forman, Reg. No. 33,694; Vincent P. Kovalick, Reg. No. 32,867; James W. Edmondson, Reg. No. 33,871; Michael R. McGurk, Reg. No. 32,045; Joann M. Neth, Reg. No. 36,363; Gerson S. Panitch, Reg. No. 33,751; Cheri M. Taylor, Reg. No. 33,216; Charles E. Van Horn, Reg. No. 40,266; and Linda A. Wadler, Reg. No. 33,218; and

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

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